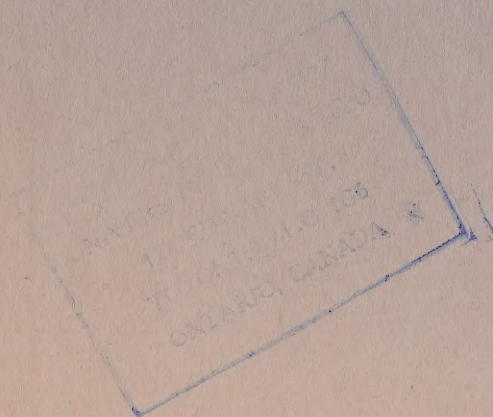


VF: WATER--FLUORIDATION

Fluorides

FACTS ON FLUORIDATION



CANADIAN DENTAL ASSOCIATION
234 ST. GEORGE STREET
TORONTO, CANADA

Revised June, 1954

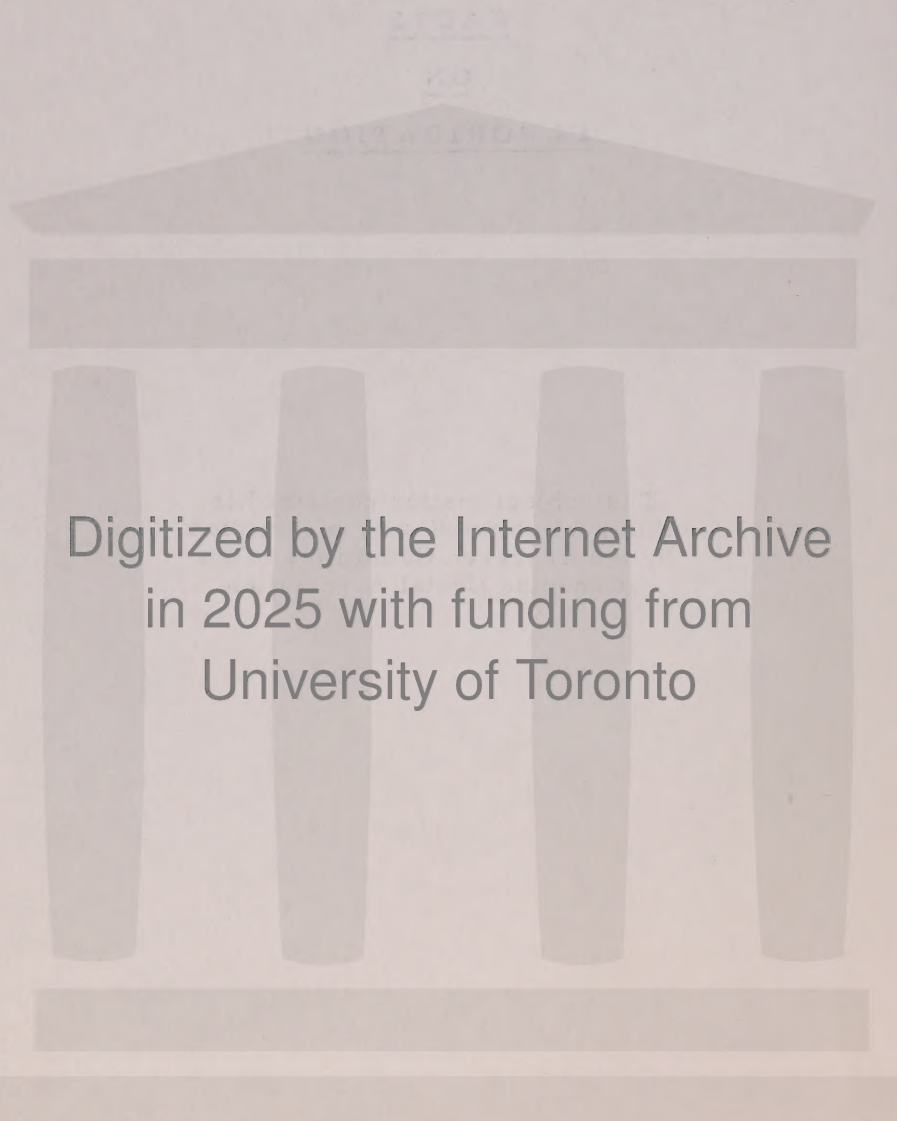
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FACTS
ON
FLUORIDATION

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FACTS ON FLUORIDATION

I. NATURAL OCCURRENCE OF FLUORINE* IN FOOD AND WATER

Most natural water supplies and many different foods contain trace quantities of fluorine. Thus, under normal conditions of living, minute quantities of fluorine are consumed in the daily diet.

The widespread occurrence of fluorine in food is shown in Table I, (page 23). Approximately 0.2 - 0.3 milligrams of fluorine are ingested daily in the food we eat (Armstrong, 1943). The amount of this fluoride absorbed is too small to have any detectable effect on the body. Only certain teas, fish and bone meal preparations contain quantities of fluoride that may be of significance in nutrition. The most significant intake of fluoride is through the medium of drinking water. The amount of water consumed by adults in temperate climates is about 1200 to 1600 cc. daily (McClure, 1943). If water contains 1.0 p.p.m. (parts per million) of fluorine, approximately 1.2 - 1.6 mg. of fluorine is consumed daily. It is evident that water containing fluorine is the major source of this trace element.

Populations in many parts of the world such as Argentina, Canada, China, England, India, Italy and the United States have for centuries been drinking water in which fluoride occurs naturally. In the United States more than 4,000,000 people have used water containing fluoride in a concentration of 3.1 - 5.0 p.p.m. for several generations. A chart locating some of the natural fluoride-bearing water supplies in Canada is appended as Appendix I and will be found on page 30.

*Fluorine is one of the most active elements of the halogen family. On account of its affinity for other elements it is seldom found free in nature. When combined with other elements to form a salt it is called a fluoride, for example, sodium fluoride.

II. ENDEMIC DENTAL FLUOROSIS (MOTTLED TEETH)

The finding that there is a relation between fluorine and dental health had its beginning in the discovery, in 1931, that high fluoride concentrations in water cause a condition known as endemic dental fluorosis (mottled teeth). This condition is due to a disturbance in the calcification of enamel and dentin and in its mildest form produces a chalky white enamel surface. As the fluoride concentration increases (4 - 8 p.p.m.), discrete or confluent pitting of the enamel surface with brown staining may occur. The severity of dental fluorosis is proportional to the concentration of fluoride in the drinking water that is consumed during that period in childhood when the teeth are being formed. Endemic dental fluorosis in a readily observable form appears only when the fluoride supply in the water exceeds 2.0 p.p.m. (Deatherage, 1941).

It was observed among children using fluoride-bearing water that the incidence of dental caries was very low, whether or not their teeth showed signs of fluorosis. This observation led to extensive epidemiological studies dealing with the relationship between fluoride and dental caries.

III. RELATION OF FLUORIDES TO DENTAL CARIES

A. In Areas where Fluoride Occurs Naturally

The low incidence of dental caries found among children living in communities whose natural water supplies contain fluoride has been clearly demonstrated by the epidemiological studies of Dean and his co-workers (Dean et al, 1941 and 1942). See Table II on page 24. The optimal concentration of fluoride (F) which affords maximum protection against dental caries with a minimum amount of dental fluorosis appears to be about 1 p.p.m. (Figure 1 - see page 28). Beyond this level there is little improvement in caries protection, and above 2 p.p.m. most of the children begin to show observable fluorosis (Dean, 1942).

It has been repeatedly demonstrated that children who have consumed fluoride free water all their lives experience almost twice as much dental decay as those children whose natural water supply contains traces of this element (Figure 2 - see page 29). This protection against dental caries due to the ingestion of the required trace of fluorides apparently extends into adult life, (Russell and Elvove, 1951). See Table III on page 25.

Since the shedding of deciduous teeth and the development and eruption of the permanent teeth is a continuous process extending up to about the 20th year of life, and because some topical effects from the passage of fluoride-bearing water over the teeth are likely, the benefits of water fluoridation are not confined to the native born population (Klein, 1948). The maximum protection is of course obtained by individuals of continuous residence.

B. In Areas where Fluoride is added

As early as 1945 certain communities, Brantford, Ontario, (Hutton et al 1951; Brown, H.K., 1952 and 1953) Newburgh, New York, (Ast, D.B. et al, 1951) and Grand Rapids, Michigan, (Cox, C.R. and Ast, D.B., 1951) adjusted the fluoride content of their water supplies by using fluoride salts fed by an automatic mechanical apparatus. These devices simulate and improve upon the process by which natural water supplies pick up their fluoride salts from the subterranean deposits of natural fluoride-bearing chemicals. The effect of this controlled fluoridation has been to reduce the dental caries attack rate in the previously fluoride deficient municipalities to the level observed in natural fluoride-bearing regions. See Table IV on page 26.

A recent survey completed by the American Dental Association (1953) indicates that one out of every nine persons in the United States is routinely drinking water containing trace quantities of added fluorine. The survey reveals that 14,266,351 persons in 771 communities are served by fluoridation programs.

IV. MECHANISM BY WHICH FLUORIDES REDUCE DENTAL CARIES

There are at least two possible mechanisms by which fluoride may protect teeth against dental caries:

- (1) Incorporation of fluoride into the tooth substance makes the tooth more resistant to acid etching. (Suess and Fosdick, 1951)
- (2) Bacteria are known to be involved in dental caries. Fluoride in suitable concentrations inhibits many bacterial enzymatic reactions. Liberation of fluoride ion from the tooth substance may inhibit certain bacteria from participating in the dental caries process. (Wright and Jenkins, 1954)

V. METABOLISM OF FLUORINE

A. Fluorine Content of Body Fluids and Tissues

(1) Bones and Teeth

The dental tissues and the skeletal system are the major storehouse for fluorine in the body. Klement (1938) states that bones of animals (including man) average 0.05 per cent fluorine in inorganic bone material. There is a strong possibility that a 'normal' increase in the fluorine content occurs in skeletal tissues and perhaps in dental tissues, with increasing age. The normal fluorine content of ribs is 0.03 to 0.14 per cent fluorine. Roholm (1937) showed that the fluorine content of the ribs of two cryolite workers (age 68 and 52) exposed to factory dust for 15 years and 8 years respectively equalled 0.65 - 0.72 per cent. Wolff and Kerr (1938) found that long bones of individuals with non-disabling fluorosis contained 0.18 - 0.29 per cent of fluoride. They concluded that the skeletal tolerance was of the order of 0.2 - 0.3 per cent of fluoride.

(2) Placenta and Mammary Secretion

Fluorides penetrate the placental barrier in small amounts only; the amount in mammary secretion is very low. According to Gardner (1952) fluorides are concentrated in the placenta. The fluoride value of 2.09 p.p.m. was found in placental tissue obtained from an area where the fluoride content of water is 1.2 p.p.m. This is compared to a value of 0.74 p.p.m. in the placental tissue obtained from areas where the fluoride concentration in water is 0.05 p.p.m.

(3) Saliva

Available evidence indicates that the excretion of fluorine through saliva is not of major importance. When radioactive fluorine is injected into the blood stream only trace amounts appear in the saliva (Wills, 1940). The fluorine content of saliva is in the order of 0.1 p. p. m. and is not influenced by

the fluorine content of drinking water up to 1.8 p. p. m. (Cox, 1952).

(4) Urine

According to McClure (1947) there is a very efficient elimination of fluorine by way of the urine. When 3.0 - 4.0 mg. of fluorine were ingested daily more than 90 per cent was eliminated by the kidney in healthy adults. The average urinary fluoride excretion by groups of young men closely approximate the concentrations that were found in the water they drank over the range of 0.2 to 4.7 p. p. m. (See Table V. on page 27.) Studies by Largent (1952) indicate that the amount of fluoride excreted by the kidneys appears to be related to the amount of fluoride previously stored.

(5) Sweat

McClure (1946) found that in a group of five young men (19 - 24 years) who were given 3.0 mg. fluorine daily, undiluted sweat contained from 0.5 - 1.8 p. p. m. fluorine. Machle and Largent (1943) found an average of 0.514 - 0.0666 p. p. m. fluorine in perspiration. This evidence suggests that sweat and insensible perspiration may account for an appreciable loss of fluorine from the body.

(6) Fluorine in Blood

A 23-fold increase in fluoride content of drinking water (0.06 - 1.36 p. p. m.) results in a 3-fold increase of blood fluorine. The maximum observed level was 0.1 p. p. m. (Smith, Gardner and Hodge, 1950).

V. METABOLISM OF FLUORINE (cont'd)

B. Balance Studies

Heyroth's (1952) data indicates that adults are in metabolic balance with respect to fluoride when the daily ingestion of fluoride is 0.44 to 0.72 mg. per day. McClure (1946) states that in young adult men there is no significant retention of fluorine when the total daily fluorine ingested did not exceed 4.0 to 5.0 mg. daily.

Retention of fluoride in babies and young growing children is a subject that has not received much study. Balance studies by Ham (1952) were carried out in five young infants. The studies indicated that the fluorine in the infants' diet was retained to some extent. The per cent retention was influenced considerably by the fluorine content of the food consumed.

VI. THE TOXICITY OF FLUORIDES IN POTABLE WATER SUPPLIES

Two aspects of this problem require consideration. One aspect is acute poisoning resulting from ingestion of large single doses of fluorides; the other is the effects of a long term ingestion of small amounts of fluoride as contained in potable waters. The former is a situation that may affect a single person or at most a very small group, whereas the latter is a public health problem.

A. Acute Toxicity

Examination of the phenomena of acute toxicity from fluorine is of value only as a possible aid in revealing what tissues or organs are most vulnerable to fluorine.

Fluorides in relatively large doses are highly toxic. Roholm (1937) estimated that the lethal dose of sodium fluoride for man was four grams. Acute symptoms may be caused by 250 mg. of sodium fluoride (Cox and Ast, 1951).

The high dosages necessary for acute fluoride poisoning could not be obtained as a result of accidental or deliberate over-fluoridation of water supplies. In order to obtain acute toxic effects it would be necessary to dump approximately eight tons of sodium fluoride into the Brantford water supply in one day. The amount actually used in the Brantford supply is about 140 pounds in one day.*

B. Chronic Toxicity

(1) Bones and Teeth

Moller and Gudjonsson (1932) in an examination of 78 cryolite (sodium aluminum fluoride) workers found that 30 complained of stiffness and

* (Based on a 5,000,000 Gallon consumption)

pain and showed x-ray evidence of osteosclerosis. It was estimated that 14 to 25.4 mg. of fluorine in dust was inhaled daily. The average deposition of fluoride was about 12 mg. per day absorbed over a period of more than 20 years. Autopsy examination of two persons who died of intercurrent disease showed osteosclerotic changes in the bones. No histopathological changes were observed in other organs.

Endemic skeletal fluorosis has been reported from China in mal-nourished persons who used water containing 5.9, 6.3 or 13.1 p.p.m. of fluoride (Lyth, 1946).

McClure (1946) in an examination of 1400 high school boys and 1700 draftees grouped according to fluoride exposure levels (0 to 1. p.p.m) in the water supply, found no significant differences in the numbers of bone fractures.

Hodges (1941) in a study of 31 persons who lived for 18 to 68 years at Bureau, Illinois, where the water contained 2.5 p.p.m. of fluorine found no evidence of skeletal fluorosis.

Children drinking waters containing 1 p.p.m. of fluoride have less than 10 per cent of their number develop a very mild degree of dental fluorosis. This is the earliest clinical manifestation of exposure to fluorides. It will not cause staining of the teeth and is not detrimental to their appearance.

(2) Other Tissues and Organs

McClure (1946) found that the data on stature and weight of young children and adolescents in fluoride and non-fluoride areas (up to 1.8 p.p.m.) revealed no differences. Pediatric studies in the Newburgh-Kingston area, including complete physical examination, blood and urine analysis, x-rays of hands, forearms and tibia and special eye and ear examinations revealed no

significant differences in any of the factors studied in children in the fluoride and non-fluoride areas (Schlesinger et al, 1953) This study covers a period of six years since introduction of fluoride into the Newburgh water supply.

The Wisconsin State Board of Health (1942) investigated the relative number of deaths from cancer, heart disease, nephritis and other illnesses in cities with varying concentrations of fluoride in the water. No significant differences were observed in areas where the fluoride ranged from 0.02 to 2.5 p.p.m.

Because of the chemical relationship between fluorine and the halogen group of elements, its possible effect on thyroid function has been studied. A study by Evans and Phillips (1938) revealed no correlation between the fluorine content of the thyroid gland and the basal metabolic rate of the patient. No relationship was observed between the iodine and fluorine content of these thyroids. The data gave no indication that fluorine played a part in human hyperthyroidism.

(3) Fluorides and Periodontal Disease

Russell and Elvove (1951) have compiled data from examinations dealing with periodontal disease in Boulder, Colorado (a non-fluoride area) and Colorado Springs (2.5 p.p.m. of fluoride in the water). The age groups studied were 20 to 44 years. The condition of the gingival tissues was assessed in detail and tooth mortality rates due to periodontal disease were calculated. No differences were reported in respect to gingival tissues. Tooth loss from periodontal disease averaged 0.72 teeth per individual in the non-fluoride area and only 0.29 teeth per individual in the fluoride area. Fewer teeth are lost from caries and hence more teeth are exposed to the risk of periodontal disease in a fluoride area. There is no evidence of any increased incidence of periodontal disease associated with fluoridation of water.

VII. TECHNICAL PROCEDURES OF WATER FLUORIDATION

The local water works staff in consultation with their provincial government authorities are qualified to determine the fluoride compound and chemical feeding apparatus most suitable for a particular municipality's needs.

The technical problems have been well discussed by the following authors:

H.F. Munroe (1953); Maier, (1952); Robertson, (1952); and Williams, (1951).

VII, LIST OF NATIONAL HEALTH ORGANIZATIONS
WHICH HAVE ENDORSED FLUORIDATION

Canada

Canadian Dental Association
Canadian Medical Association
Canadian Public Health Association
Canadian Society of Dentistry for Children
The Dental Public Health Committee of the Ontario
Dental Association
The Executive Council of the Toronto Academy of
Dentistry
The Health League of Canada
The Ontario Public Health Association
Toronto Academy of Medicine

United States

American Association of Public Health Dentists
American Dental Association
American Hospital Association
American Medical Association
American Nurses' Association
American Public Health Association
American Society of Dentistry for Children
The Commission on Chronic Illness
National Research Council (U. S. A.)
State and Territorial Dental Health Directors
State and Territorial Health Officers Association
United States Public Health Service

IX. STATEMENT OF THE CANADIAN DENTAL ASSOCIATION
ON FLUORIDATION

Motion passed by Board of Governors of the Canadian
Dental Association respecting Approval of Fluoridation:

WHEREAS tooth decay, by affecting the vast majority of people in Canada has come to be recognized as one of the major public health problems of our time, and,

WHEREAS many thousands of Canadians and millions of people elsewhere have consumed during their total life times, water fluoridated to approximately one part of fluoride to a million parts of water from underground deposits, and have thereby benefited by a reduction of about two thirds in the attack rate of tooth decay without any ill-effects discoverable by either the dental or medical professions, and,

WHEREAS the effects of adjusting the fluoride content of communal water supplies to approximately one part per million have been studied extensively in their dental and medical aspects for more than eight years, revealing in every instance the same beneficial dental health results that have been known for over 20 years to accrue from consuming water fluoridated from underground deposits, and with the same freedom from any systemic ill-effects,

Therefore be it resolved:

THAT the Canadian Dental Association recommends to the people of Canada that communities having a public water supply, adopt a procedure for water fluoridation best suited to their local needs, and for this purpose seek competent dental, medical, and engineering advice.

X. FLUORIDATION IN CANADA

A. Communities in Canada which have started Fluoridation*

Brantford, Ontario.

Fort Erie, Ontario

Thorold, Ontario

Sudbury, Ontario

Chalk River, Ontario

Oshawa, Ontario

Moose Jaw, Sask.

Assiniboia, Sask.

B. Communities in Canada which have approved Fluoridation*

Windsor, Ontario

Hawkesbury, Ontario

Regina, Sask.

Saskatoon, Sask.

Prince Albert, Sask.

*From a Questionnaire sent to the Provincial Deputy Ministers of Health, April, 1954, by the Department of Health and Welfare, Victoria.

XI. SUMMARY

1. Most natural water supplies and many different foods contain fluorine. The most significant source of fluorine from a standpoint of human consumption is water. Concentration of fluorine in water may vary from traces to excessive amounts. Populations in many parts of the world have for centuries been drinking water in which fluoride occurs naturally.
2. There is approximately a 60 per cent reduction in dental caries where a desirable amount of fluoride ion, whether naturally occurring or the result of supplement, exists in the drinking supply. The desirable concentration of fluorine in water, based on its ability to reduce the incidence of dental caries without any undesirable effects is in the order of one part of fluoride ion per one million parts of water. Higher concentrations of fluorine produce no added reduction in dental caries but result in dental fluorosis.
3. There is no evidence of detrimental effects on the health of individuals drinking water containing fluorine at the level of intake of 1 p.p.m. Studies of vital statistics of common major diseases, and of maternal and newborn death rates, all confirm the safety of a fluoridation program.
4. Most of the fluoride consumed at the level of 1 p.p.m. is excreted by the kidneys and sweat. A minimal amount, far below the fluorosis threshold, is stored, in bones and teeth.
5. Most health organizations of recognized scientific standing have endorsed the efficacy and safety of fluoridation. A recent survey indicates that a total of 14,266,351 persons in 771 communities or one out of nine persons in the United States is served by fluoridation programs.
6. Scientific studies offer an impressive body of evidence that 'bringing the fluoride concentration in communal water supplies to that known to be

optimal for dental health is a prophylactic public health measure which has an ample margin of safety'.

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* Also available at the Canadian Dental Association Headquarters.

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61. Wright, D.E. and Jenkin, G.N. The effect of fluoride on the acid production of the saliva - glucose mixture. Brit. Dent. Jour. 96:30:54.

TABLE I

FLUORINE CONTENT OF FOODS

Food	Fluorine, parts per million	Food	Fluorine, parts per million
Fluorine reported in food as consumed			
Milk	0.07-0.22	Pork Chop	1.00
Egg white.....	0.00-0.60	Frankfurters	1.70
Egg yolk	0.40-2.00	Round steak	1.30
Butter	1.50	Oysters	1.50
Cheese	1.60	Herring (smoked)	3.50
Beef	∠ 0.20	Canned shrimp	4.40
Liver	1.50-1.60	Canned sardines	7.30-12.50
Veal	∠ 0.20	Canned salmon	8.50- 9.00
Mutton	∠ 0.20	Fresh fish	1.60- 7.00
Chicken	1.40	Canned macherel	26.89
Pork	∠ 0.20		
Fluorine reported in dry substance of food			
Rice	∠ 1.00	Honey	1.00
Corn	∠ 1.00	Cocoa	0.50- 2.00
Corn (canned).....	∠ 0.20	Milk chocolate	0.50- 2.00
Oats	1.30	Chocolate (plain)	0.50
Crushed oats.....	∠ 0.20	Tea (various brands*) ..	30.00-60.00
Dried beans	0.20	Cabbage	0.31- 0.50
Whole buckwheat	1.70	Lettuce	0.60- 0.80
Wheat bran	∠ 1.00	Spinach	1.00
Whole wheat flour	1.30	Tomatoes	0.60- 0.90
Biscuit flour.....	0.00	Turnips	∠ 0.20
Flour	1.10-1.20	Carrots	∠ 0.20
White flour	1.00	Potato (white)	∠ 0.20
Ginger biscuit	2.00	Potato (sweet)	∠ 0.20
Rye bread	5.30	Apples	0.80
Gelatin	0.00	Pineapple (canned)	0.00
Dextrose	0.50	Orange	0.22

* Analysis of tea leaf. A cup of tea contains about 0.12 mg. of fluorine.

Source: McClure, F.J., National Inst. of Health Bulletin, 172, 1939.

TABLE II

Summary of Dental Caries Findings in 7,257 Selected White School Children
Age 12 to 14 years, in 21 cities of 4 States
in Relation to the Fluoride (F) Content of the Public Water Supply

City and State	No. of Children Examined	Percent of Children Caries Free	No. of D.M.F. Teeth per Child with Caries Experience	F. Conc. (p.p.m) Public Water Supply
Galesburg, Ill.	273	27.8	2.36	1.9
Colorado Springs, Colo.	404	28.5	2.46	2.6
Elmhurst, Ill.	170	25.3	2.52	1.8
Maywood, Ill.	171	29.8	2.58	1.2
Aurora, Ill.	633	23.5	2.81	1.2
East Moline, Ill.	152	20.4	3.03	1.2
Joliet, Ill.	447	18.3	3.23	1.3
Kewanee, Ill.	123	17.9	3.43	0.9
Pueblo, Colo.	614	10.6	4.12	0.6
Elgin, Ill.	403	11.4	4.44	0.5
Marion, Ohio	263	5.7	5.56	0.4
Lima, Ohio	454	2.2	6.52	0.3
Evanston, Ill.	256	3.9	6.73	0.0
Middletown, Ohio	370	1.9	7.03	0.2
Quincy, Ill.	330	2.4	7.06	0.1
Oak Park, Ill.	329	4.3	7.22	0.0
Zanesville, Ohio	459	2.6	7.33	0.2
Portsmouth, Ohio	469	1.3	7.72	0.1
Waukegan, Ill.	423	3.1	8.10	0.0
Elkhart, Ind.	278	1.4	8.23	0.1
Michigan City,	236	0.0	10.37	0.1

Source: Dean, H.T., et al, 1941

TABLE III

Comparison of Average No. of Decayed, Missing and Filled Permanent Teeth
in Adult Natives of Boulder, and Colorado Springs, Colorado,
excluding third Molars.

Age Group Years	Boulder (F concentration . 1 ppm)		Colorado Springs (F concentration 2.5 ppm)		Per Cent reduction in Colorado Springs
	Number of Persons	Mean no. of D.M.F. Teeth *	Number of Persons	Mean no. of D.M.F. Teeth *	
20-24	51	13.8	72	5.2	62.3
25-29	41	16.0	101	6.2	61.2
30-34	29	16.3	82	6.7	58.3
35-39	22	20.4	75	7.6	62.7
40-44	12	19.1	55	8.7	54.5

* Decayed, Missing or Filled Teeth omitting loss due
to periodontal Disease and accidents

Source: A.L. Russell and E. Elvove (1951)

TABLE IV

RESULTS OF FLUORIDATION STUDIES

City	Date Started	Report Period	Age Group	Per Cent of Reduction in decayed, missing and filled teeth	
				Perm.	Primary
Brantford, Ontario Canada	June 1945	1948-1953	6- 8	55%*	35%
			9-11	39%	17%
			12-14	28%	
Evanston, Illinois	February 1947	After 12-23 months	6	50%	
			7	33%	
			8	22%	
		After 47-58 months	Same group	71%	7%
				56%	0
Grand Rapids, Michigan	January 1945	After 5 years			
			4		41%
			5		53%
			6	66%	42%
			7		25%
			8		15%
			9	39%	
			13	26%	
Lewiston, Idaho	June 1947	After 3 years	7	58%	
			8	35%	
			9	25%	
Madison, Wisconsin	June 1948	After 3 1/2 years	Kinder- garten		48%
Marshall, Texas	May 1946	After 29 months	6	47%	
			All School Ages	23%	
Newburgh, New York	May 1945	For primary teeth 1945-1949	5		60%
			6	69%	46%
			7	68%	28%
			8	40%	19%
		For permanent teeth 1944-1952	9	40%	
			10	42%	
			11	39%	
Sheboygan, Wisconsin	March 1946	After 5 1/2 years	12	35%	
			5- 6		54%
			9-10	30%	
			12-14	23%	

* The first permanent molars of the Brantford children born subsequent to the initiation of fluoridation in June 1945, appear to show a resistance to caries comparable to that of the teeth of the children of the same age in Stratford where the water has contained 1.3 p. p. m of fluoride since 1917.

SOURCES: Council on Dental Health, Am. Dent. A., May 1, 1952, Report on Brantford Fluoridation Study, Dept. of Nat. Health & Welfare, Ottawa, Aug. 1953. Journal Dental Research 31: 346, 1952, Oral Surg., Oral Med. and Oral Path. 6:114, 1953.

TABLE V

FLUORINE CONTENT OF URINE STUDIED IN RELATION TO
FLUORINE IN FLUORIDE DRINKING WATER

Location	Fluorine in water	Fluorine in urine	Number of specimens represented	Comment
Amarillo, Texas	ppm 4.7	ppm 4.6	26	High school boys age 16-18
Amarillo, Texas	4.7	4.0	42	Selectees, Lubbock induction center
Airfield, Lubbock, Texas	5.1	4.0	50	Service men station- ed at airfield
Lubbock, Texas	3.8	3.8	52	High school boys age 16-18.
Lubbock, Texas	3.8	4.2	21	Texas Tech. College men age 17-21
Lubbock, Texas	3.8	3.7	108	Selectees, Lubbock induction center
Glider field, Lubbock, Texas	2.0	2.0	16	Service men station- ed at Glider field
Galesburg, Ill.	1.9	1.8	173	High school boys age 15-17
Monmouth, Ill.	1.7	1.4	156	High school boys age 15-17
Joliet, Ill.	1.3	1.0	21	Selectees, Chicago induction center.
Aurora, Ill.	1.0	0.9	170	High school boys age 15-17
Elgin, Ill.	0.7	0.7	170	High school boys age 15 - 17
Rural central Ind.	0.5*	0.7	109	Selectees, Indiana- polis induction center
Oklahoma City, Okla	0.5	0.6	26	High school boys age 16-18
Indianapolis, Ind.	0.2	0.4	121	Selectees, Indiana- polis induction center
Chicago, Ill.	0.1	0.3	60	Selectees, Chicago induction center
Quincy, Ill.	0.1	0.3	85	High school boys age 15-17
Washington, D.C.	0.0	0.4	202	Selectees, Ft. Myer induction center
Washington, D.C.	0.0	0.3	65	High school boys age 15-17
Little Rock, Ark.	0.0	0.3	26	High school boys age 15-18
Waukegan, Ill.	0.0	0.4	144	High school boys age 15-17
New Hampshire	0.0	0.3	174	Selectees, Manches- ter induction center

*Estimated average for fluorine in waters at this area

Source: McClure, 1946, National Institute of Health, Division of Physiology Dental
Research Section, Bethesda, Maryland.

FIGURE 1

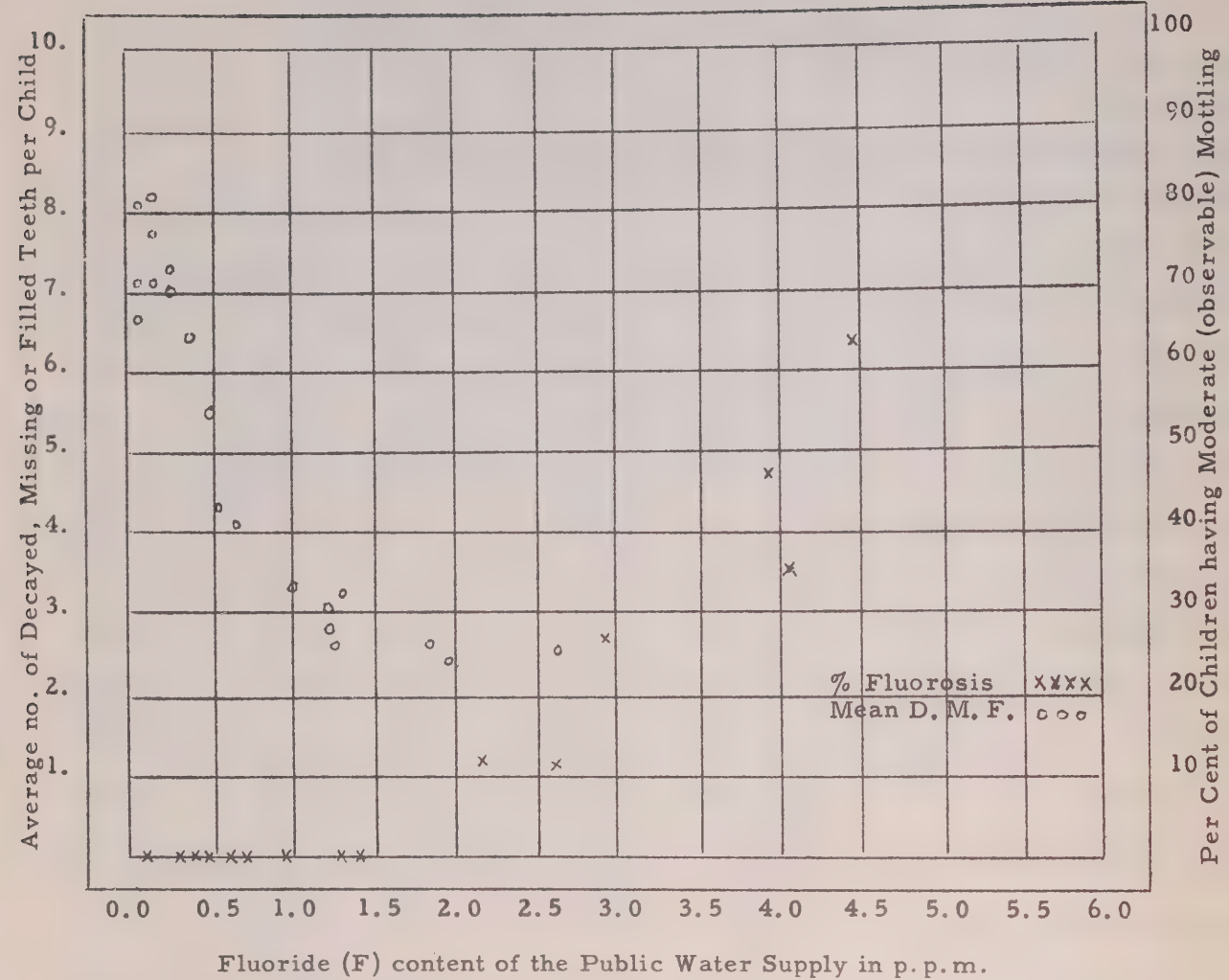


Figure 2. Relationship of Fluoride (F) control of Public Water Supply in p.p.m. the average number of decayed, missing and filled teeth per child, age 12 to 14 years and the prevalence of moderate, (observable) brown mottling among children age 9 to 12 years in cities of U.S.A.

Source: H.T. Dean, 1941, and Dean et al, 1941, 1942.

FIGURE 2

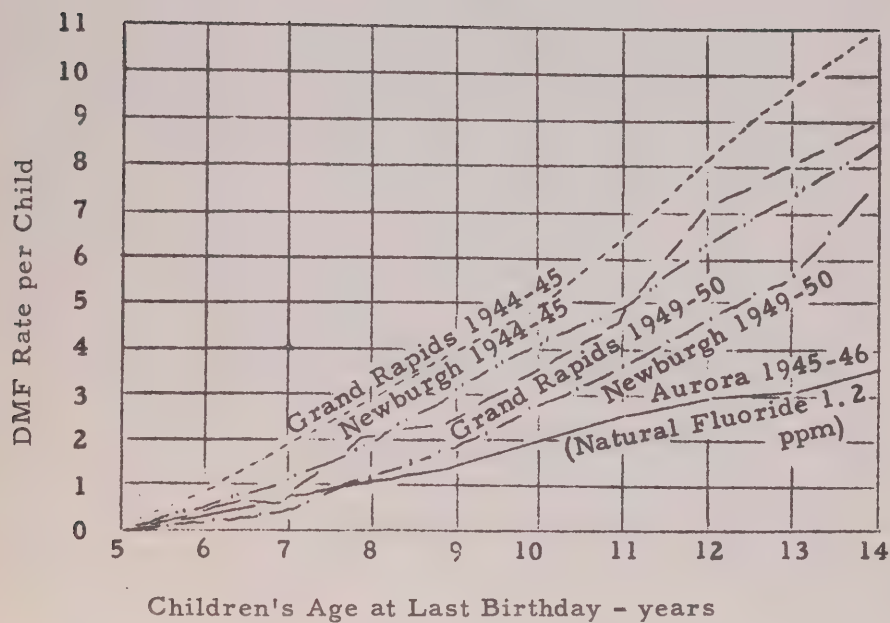


Figure 2. Permanent Teeth per Child in Controlled and Natural Fluoride Areas

The Newburgh and Grand Rapids data for the years 1944-50 are plotted against the DMF rates in Aurora, Ill., a community with a natural concentration of 1.2 ppm. fluoride in its water.

Source: Cox, C.R. and Ast, D.B., 1951

APPENDIX I

LIST OF SOME AREAS IN CANADA
CONTAINING NATURAL FLUORIDE
IN MUNICIPAL WATERS

AMOUNTS OF NATURAL FLUORIDE IN MUNICIPAL WATERS

<u>Place</u>	<u>Year</u>	<u>Source</u>	<u>Fluoride Content</u> ppm*
<u>Province of British Columbia</u>			
Bralorne, B.C.	1952		0.1
Boston Bar, B.C.	1946	Stoyoma Creek	0.01
Cloverdale, B.C.	1952		1.2
Creston, B.C.	1947	Arrow Creek	0.1
Enderby, B.C.	1948		0.25
Fort Steel, B.C.	1949		0.1
Fort St. John, B.C.	1949	Charlie Lake	0.02
Kelowna, B.C.	1952	North Okanagan Lake	0.2
Kimberley, B.C. (airport)	1949	Deep Well	0.07
McBride, B.C.	1948	Dominion Creek	0.10
North Vancouver, B.C.	1949	Lynn Creek	0.05
North Kamloops, B.C.	1948	South Thompson River	0.07
Oliver, B.C.	1950	Shallow Well	0.5
Summerland, B.C.	1950	Headwaters Lake	0.2
Sidney, B.C.	1948	5 Wells and a spring	0.25
Trail, B.C.	1949	Columbia River	0.1
Vernon, B.C.	1948	Kalamalka Lake and mountain springs	0.1
Williams Lake, B.C.	1950		0.1
Yale, B.C.	1949		0.03
<u>Province of Alberta</u>			
Beaver River, Alta.			0.1
Bonnyville, Alta.		Shallow Well	0.35
Cardston, Alta.		From River	0.3
Lacombe, Alta.		Deep Well	1.0
Mirror, Alta.		Well	0.5
Saunders Lake, Alta.			0.4
St. Paul, Alta.			0.07
<u>Province of Saskatchewan</u>			
Prince Albert, Sask.		North Saskatchewan River	0.12
Shaunavon, Sask.		Well	0.1
Swift Current, Sask.		Swift Current Creek	0.25
Weyburn, Sask.		Souris River	0.18
Yorkton, Sask.		3 Wells	0.2
<u>Province of Manitoba</u>			
Winnipeg, Man.		Shoal Lake, Lake of the Woods	0.25

*Parts per million.

<u>Place</u>	<u>Year</u>	<u>Source</u>	<u>Fluoride Content</u> ppm.
<u>Province of Ontario</u>			
Alymer, Ont.		Well No. 2	1.0
Bradford, Ont.		Artesian Well	5.5
Caledonia, Ont.		Wells (water softened)	0.60
Clinton, Ont.		Well	0.8
Coburg, Ont.		Springs	.05
Dresden, Ont.		Well	2.0
Dunnville, Ont.		Grand River	0.2
Essex, Ont.		Boone Well	2.5
Etobicoke Twp., Ont.		Deep Wells	.05
Fergus, Ont.		Well	0.6
Galt, Ont.		Civic Well	.38
Georgetown, Ont.		Deep Well	0.2
Gravenhurst, Ont.		Wells	.21
Guelph, Ont.		Park Street Well	0.3
Hamilton, Ont.		Lake Ontario	0.1
Hagersville, Ont.		Deep Well	1.2
Ingersoll, Ont.		Springs	0.05
Kitchener, Ont.		Wells	.05
Leamington, Ont.		Wells	0.5
Lindsay, Ont.		Scugog River	.07
London, Ont.		Norton St. Well	0.7
London, Ont.		(Springs) Springback	0.1
London, Ont.		Foster Wells	0.3
Lucknow, Ont.		Wells	2.0
Meaford, Ont.		Georgian Bay	0.1
Niagara-on-the-Lake, Ont.		Niagara River	0.1
North York Twp., Ont.		Well Plant No. 2.	0.05
Oakville, Ont.		Lake Ontario	.08
Orillia, Ont.		Well	.05
Oshawa, Ont.		Lake Ontario	.10
Paris, Ont.		Springs	.05
Peterborough, Ont.		Otonabee River	.07
Petrolia, Ont.		Lake Huron	0.05
Port Colborne, Ont.		Lake Erie	0.15
Port Dover, Ont.		Springs	0.1
Port Credit, Ont.		Lake Ontario	0.1
Port Elgin, Ont.		Wells and Springs	0.2
Preston, Ont.		Well No. 2	0.1
Ridgetown, Ont.		8 Wells	1.2
Scarborough Twp., Ont.		Lake Ontario	0.09
Seaforth, Ont.		Wells	0.8
Shelburne, Ont.		Well	1.5
Simcoe, Ont.		Wells and Springs	0.1
Sioux Lookout, Ont.		Pelican Lake	0.05
South River, Ont.		Springs	0.1
Stamford Twp., Ont.		Wells	0.1
St. Catharines, Ont.		Welland Canal	0.1
St. Thomas, Ont.		Kettle Creek	.25
Stirling, Ont.		(Gravel and Sand) Well	0.25
Stirling, Ont.		Rock Well	0.15
St. Mary's Ont.		Wells	1.0

Province of Ontario (Cont'd)

<u>Place</u>	<u>Year</u>	<u>Source</u>	<u>Fluoride Content</u> ppm.
Stratford, Ont.		Wells	1.6
Tara, Ont.		Well	.80
Tavistock, Ont.		Spring,	0.05
Tecumseh, Ont.		Detroit River	0.1
Teeswater, Ont.		Artesian Well	0.5
Thornbury, Ont.		Beaver River	0.10
Thorold, Ont.		Welland Canal	.15
Thorold Twsp., Ont.		Welland Canal	0.05
Tilbury, Ont.		Lake St. Clair	0.05
Tillsonburgh, Ont.		Two gravel wells	0.15
Trenton, Ont.		Springs and Wells	.05
Tweed, Ont.		Foster Dairy Well	.05
Uxbridge, Ont.		Wells	.04
Walkerton, Ont.		Wells and Springs	1.5
Waterloo, Ont.		Seagram Well	0.40
West, Ont.		Lake Erie	0.4
Woodstock, Ont.		Gravel Wells	.15

Later Analysis

Ingersoll, Ont	1953	(a) Well	1.8
		(b) Well	1.8
St. Mary's, Ont.	1953	Well	1.2
Woodstock, Ont.	1953	(a) Well	0.3
		(b) Well	0.3
		(c) Well	0.3

Source: Department of National Health and Welfare, Ottawa, Canada.

26 August 1953.

APPENDIX II

REPRINTS

THE TOXICITY OF FLUORIDES IN RELATION TO THEIR USE IN DENTISTRY

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It has been our purpose to review the toxicology of fluorides only in the aspects related to dental health. The list of dental uses of fluorides is growing and has already included the following surprisingly large number of items: (1) Fluoridization of water and related pre-eruptive procedures for the prevention of dental caries. (2) Topical application of fluorides for control of dental caries. (3) Fluoride pastes to desensitize dentin. (4) Toothpastes and powders. (5) Mouth wash. (6) Fluoride plus vitamin tablets. (7) Chewing gum.

With the increased use of fluorides, it is proper to insist that due attention be paid to the possible hazards and to insist that there be a large factor of safety. Fluorine and its compounds have long been known as poisons. In the following discussion, the toxic effects of fluoride are grouped under four main headings: Acute Poisoning, Chronic High-Grade Poisoning, Chronic Low-Grade Poisoning, and Local Action. In each case, after the toxic effects have been described, an evaluation has been made of the possibility of such effects appearing in conjunction with the use of fluorides in dentistry.

It is our intent to indicate the safety of the therapeutic uses of fluorides, and it is not our intent to warn against the uses of fluorides in dentistry. This discussion, however, should alert the users to the dangers of carelessness and misuse, dangers to both the subjects and the operators.

Objections to the uses of fluorides in dentistry have come from various sources. These have been mainly from the specialists in various fields who are uninformed about the proved possibilities of fluorides. Those who have competing procedures have advanced their wares by attacks on fluorides. Some who have seen only the bad effects of fluorides refuse to accept the good. There have been dire warnings of bad effects, characteristically naming nothing specific. It has been the vogue to proceed cautiously in the fluoridization of water and such caution implies more the fear of the unknown than doubt of the benefits.

The word "fluorine" as used in this paper refers to fluoride ions or the fluorine portion of a compound containing the element.

Extensive reviews of the toxicology of fluorine are available and many of the papers on mottled enamel and on dental caries present evaluations of the literature on fluorine toxicity. Symposia have dealt with the whole problem of fluorine in its relations to dental health with consideration of its toxicity, and McClure has summarized knowledge of fluoride effects published during the period 1934 through September 1948.

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The opinions expressed are those of the authors and do not necessarily reflect the opinions of the Council on Dental Therapeutics.

Acute Toxicity

Effects of Oral Doses on Man. --- Fluorides rank among the substances whose ingestion in small amounts can cause death within a few hours. Rabuteau administered sodium, potassium, ammonium and other fluorides to cats, dogs, rabbits and frogs and noted salivation and vomiting. For extension of the findings to man he took by mouth 0.25 Gm. of sodium fluoride in 25 ml. of water. (This is a 1 per cent solution of sodium fluoride or approximately 4,500 ppm. as fluoride ion. It is approximately 1 fluidounce of half the 2 per cent strength recommended for topical application of fluorides.) He noted a slight nausea with epigastric sensations which lasted about five hours. Salivation was intense for about a half hour and noticeable up to one and one-half hours. He noted an itching sensation in trunk, hands and feet that lasted about a week. It is important to note that Rabuteau swallowed approximately 1 fluidounce of a 1 per cent sodium fluoride solution; that is, one of half the strength recommended for topical application of sodium fluoride.

Baldwin swallowed sodium fluoride experimentally, in increasing doses. He reported:

0.03 gm. swallowed with some bread produced no effect. Neither did 0.09 gm. taken one hour later, except a little salivation. 0.25 gm., however, taken two days afterward on an empty stomach, produced nausea in two minutes. This gradually increased in severity for twenty minutes when the period of greatest intensity was reached. There was a largely increased flow of saliva and some retching but no vomiting occurred at that time though the desire was very great. The nausea gradually subsided so that luncheon could be eaten (without relish), but no vomiting took place immediately on its completion which was two hours after taking the poison. Slight nausea continued throughout the following day but disappeared on the second day.

That Rabuteau and Baldwin were fortunate is indicated by the findings of Gettler and Ellerbrook. They analyzed the vital organs and tissues from five fatal cases of fluoride poisoning. Since all the materials were not submitted for analysis, they supplemented their data with analyses of tissues from dogs experimentally poisoned. They found the fluorine contents of the organs of the two species after acute fluoride poisoning to be within the same range and no difference whether death was caused by sodium fluoride or fluosilicate. The fluorine content of the urine was highly variable.

Following a brief review of estimates by others of the minimum lethal dose of fluorine they wrote:

The reason why such wide variations as to the lethal dose exists may be (a) the amount of fluorine actually taken by the subject is only a guess; (b) some of the ingested fluorine is lost in the vomitus; (c) the fluorine remaining in the gastro-intestinal tract (unabsorbed) has no bearing on the cause of death; that part of the poison which has been absorbed into the circulation and tissues is solely responsible for the death of the individual; (d) fluorine is a very rapidly excreted in the urine.

Gettler and Ellerbrook then calculated from the analyses of human and dog tissues that death could be caused in a 140 pound man by absorption of as little as 105 mg. of fluorine. The dosage taken by mouth by both Rabuteau and Baldwin was approximately 110 mg; the amount absorbed is unknown.

Approximate Lethal Dose for Man --- It is unnecessary to stress the difficulty of estimating accurately the dose of fluoride to kill the average man. In animals, for example in the rat, the LD50 (dosage from which 50 per cent of the animals die) is of the order of 50 mg. per kilogram of body weight. Since fluoride is one of the general protoplasmic poisons, it may well be that an average fatal dose for man is of the same order of magnitude. It would be impossible to cite all of the estimated doses in fatal poisoning cases that have been recorded in the literature. In the brevity required by this review, instead, a few typical examples are cited in Table 1.

Table 1. --- Examples of the relation of various dosages of fluorides to the lethal dosage in man -

Probable dose	Effect	Compound
100 mg. or more	Death predicted	Sodium fluoride (fluosilicate)
0.2 - 0.6 Gm.	71 cases with recovery	Sodium Fluoride
0.7 --1.0 Gm.	Fatal	Sodium fluosilicate
1 Gm. or more	60 fatal cases 52 survived	Fluoride and Fluosili- cate
5 Gm.	Fatal	Fluoride or Fluosili- cate
5-- 9 Gm.	Recovery	Sodium fluoride
5--10 Gm.	47 fatal of 263 cases	Sodium fluoride
95 per cent paste in water, 50-80 Gm.	Recovery	Sodium fluoride

It is difficult to judge the minimum lethal dose from the above, mainly because the estimation of the doses is quite uncertain and fluoride has been ejected in unknown amount through vomiting. Roholm's opinion that 4 Gm. is the minimum amount of sodium fluoride known to have caused death of an adult has been widely accepted. Black, Kleiner and Bolker claimed that oral doses of 20 to 50 mg. of sodium fluoride given four times a day to children 3 1/2 to 6 years of age, or 80 mg. doses given four times a day to adults, were not toxic. The sodium fluoride was given with a suspension of aluminum hydroxide. Sharpless has shown that an aluminum salt fed in excess of sodium fluoride prevents mottling of the enamel of rat incisors. Black, Kleiner and Bolker stated "If taken alone, sodium fluoride causes gastritis and regurgitation."

Mechanism of Acute Fluoride Poisoning. --- While the mechanism of acute fluoride poisoning is still obscure, studies from a variety of sources have indicated how some of the effects arise. The nausea, vomiting and the diarrhea in some cases may be attributed to the ingestion of the hypertonic salt solution which is irritating to the mucosa of the stomach. The local action of fluorides on the mucosal tissues certainly contributes to these effects.

When absorbed, fluoride forms strong complexes with calcium; for example, Rabinowitch described a case of suicide by ingestion of sodium fluoride. The subject did not vomit. He showed spasms of the hands and feet and died of respiratory failure three hours and five minutes after ingestion of the poison. A blood sample taken a few minutes before death showed 2.6 mg. of calcium per 100 ml. of serum, believed by Rabinowitch to be the lowest ever observed in man. Normal is 9 to 11.5 mg. The low blood calcium may be the basis for the twitchings observed in severely poisoned individuals.

Probably the most important actions of fluorides are those on enzymes. Some of the basic and necessary metabolic processes in the cell are stopped by concentrations of fluoride such as are found in acute poisoning. These changes are comparable to those seen in high-grade anoxia and are the basis for describing fluorides as general protoplasmic poisons.

Treatment of Acute Fluoride Poisoning. --- Roholm says of fluoride poisoning:

On the whole, the prognosis must be characterized as bad; the mortality is high. Whether or not there is vomiting is a matter of vital importance to the prognosis. It is presumable that the quantity and nature of the stomach contents also have some bearing. It is possible that an existing anacidity reduces the possibility of absorption and thereby improves the prognosis.

On the whole, no definitely effective treatment has been used. The rational therapy is intravenous injection of a soluble calcium salt, to which must be added gastric lavage and peroral administration of a solution of calcium chloride, perhaps milk. Treatment must be commenced quickly to have any chance of being effective.

For treatment of acute fluoride poisoning by mouth, Rabinowitch recommended thorough washing of the stomach with lime water or a weak solution of calcium chloride if lime water is not immediately available. If neither is available, water should be used repeatedly in small amounts. He recommended intravenous injection of a 10 per cent calcium gluconate solution without delay on appearance of any signs suggestive of tetany, or very cautious injection of a more dilute solution of calcium chloride if the gluconate is not immediately available.

Peters reported the case of a 16 year old girl who swallowed with suicidal intent:

... about 4 ounces of a thicker-than-cream suspension of 95 per cent sodium fluoride in water (estimated to have been 50-80 gm.), the largest dosage from which a human has been known to recover. Undoubtedly early vomiting ejected much of this.

Peters stressed the use of lime water by gastric lavage and calcium gluconate for intravenous injection for relief of acute poisoning by ingested fluoride. He followed the suggestions of Rabinowitch in the emergency described above and credits Maletz, in 1935, as first clearly recognizing the importance of calcium therapy, though Stanton and Kahn, in 1915, used about a gallon of solution of lime water and calcium chloride for washing the stomach in the successful treatment of a 19 month old girl who had swallowed a roach powder containing about 50 per cent sodium fluoride.

The recommendations of Peters are as follows:

1. Act quickly. Fluoride may kill in a few minutes, and 3 to 4 hours after ingestion is the most frequent reported lethal interval.
2. Start intravenous therapy with glucose in normal saline promptly, both to maintain blood and sugar in case of hepatic glycogen depletion, and to have a venous channel available for transfusion. Shock may kill despite calcium.
3. Wash the stomach gently with saline, or preferably with lime water, and then give lime water at frequent intervals.
4. Have calcium available for intravenous administration and watch closely for signs of tetany. Tetanic death is often rapid.
5. Maintain high urine volume with parenteral fluid.
6. Wash away vomitus, feces and urine promptly to prevent external burns.

The identification of symptoms of acute fluoride poisoning and recommendations for treatment given by the Council on Dental Therapeutics in Accepted Dental Remedies are as follows:

Symptoms --- Nausea and vomiting; burning, cramp like abdominal pains; diarrhea. Sometimes tremors or convulsions. Greyish blue cyanosis. Urine and blood show presence of fluoride.

Treatment --- Copious gastric lavage with limewater or 1 per cent calcium chloride solution. Calcium gluconate 1 Gm (10 cc. of 10 per cent) intramuscularly or calcium chloride 1 Gm. (10 cc. of 10 per cent) in water, intravenously. Carbon dioxide-oxygen inhalation, or artificial respiration if necessary. External heat. Intravenous glucose or normal saline if necessary.

Is Use of 2 per cent Sodium Fluoride Solution Hazardous?
In our opinion, the application of 2 per cent sodium fluoride in water solution topically is perfectly safe under the conditions of application in the dental office by the dentist or dental hygienist. It has been estimated that at most 2 cc. of the 2 per cent solution are used in a single application. This volume would contain 20 mg. of fluorine (40 mg. of sodium fluoride), most of which is rinsed from the teeth and ejected from the mouth if the customary practice as described by Knutson is followed. Even if the patient swallowed the entire amount, there would be no physiological effect. The patient would not be nauseated or harmed.

The 2 per cent solution of sodium fluoride should never under any circumstances be placed in the home. The 2 per cent aqueous solution of sodium fluoride is colorless, odorless and has only a salty taste. Ten cubic centimeters of this solution accidentally drunk by a baby would give a dose of 100 mg. of fluorine -- the lethal dose cited by Gettler and Ellerbrook for an adult. If bottles of 2 per cent sodium fluoride solution are permitted in homes, it will only be a matter of time before records of children's deaths will be found in the dental and medical literature. The 2 per cent solution of sodium fluoride is too toxic to be permitted in homes.

Chronic Poisoning: High-Grade

The classical effects of chronic poisoning seen industrially, and in those ingesting drinking water with excessive concentrations of fluorides, are stiffness of the joints, exostoses, moth-eaten bones, calcification of the ligaments and, of special interest to dentists, changes in the roentgenograms of the jaw bone characterized by heavy trabeculae.

Stiff Backs. --- Shortt, Pandit and Raghavachari observed stiffness of the backs of individuals over 30 years of age in districts near Madras, India. It was a common belief that the condition derived from the water supply. Shortt and his colleagues noted severe mottled enamel and found from 0 to 10 ppm. fluorine in the waters. Pandit, Raghavachari, Rao and Krishnamurti estimated on the basis of 6 pints of daily water ingestion, that an intake of 5.4 mg. of fluoride produced a slight incidence of stiff backs; in districts with the most extreme cases the estimates ranged up to 24 mg. They said "bone affections were fairly prevalent" in a town "with a fluoride content of only 2 ppm. in their water supply." Osteosclerosis has been reported associated with mottled enamel by Capizzano, Paterson Toledo, Megy and Valotta; Capizzano, Valotta and Megy, Mascheroni, Munos and Reussi. Ockerse found 8 cases of osteoporosis in South Africa associated with mottled enamel from 12 ppm. fluorine in the water supply. Kemp, Murray and Wilson described two cases with skeletal changes associated with severe mottled enamel. Linsman and McMurray found severe osteosclerosis in a man, age 22, with a history of exposure to 12 ppm. fluorine in water. This case at autopsy showed a cystic condition of one kidney injury and atrophy of the other. There was a history of kidney injury at 15 years. They speculated as to whether the fluorine had aggravated the kidney injury or retention of fluorine had promoted development of osteosclerosis. Lyth described four cases of spondylitis in Chinese associated with mottled enamel and fluorine in the drinking water up to 13 ppm.

Although the mechanism by which high-grade chronic fluorine poisoning develops has not been described, attention should be drawn to the fact that all of the changes are associated with derangements in mineral metabolism. It has been known for some time that fluoride is a powerful poison of the phosphatase essential for calcification. Perhaps this action is responsible for the development of crippling fluorosis.

Daily Fluoride Intake Associated with Chronic High-Grade Fluorosis. --- From analyses of the urinary excretion of fluoride by cryolite workers in Denmark, the opinion has been stated that crippling fluorosis develops in individuals whose intake of fluoride exceeds 20 mg. per day for a period of 10 to 20 years. The fluoride intake of the persons referred to above who developed crippling fluorosis from drinking fluoride-rich waters is unknown, although amounts of the order of 20 mg. or more per day are plausible.

McClure has reviewed the literature on the excretion of fluoride and has concluded that at least 90 per cent of ingested fluoride appears in urine, feces and sweat when the amounts taken are in the ranges proposed for fluoridization of water. Certainly there is fluoride retained by the bones as there is ample evidence that the fluorine content of bones is increased with age. There are available reliable methods for the estimation of urinary fluorides. Consequently, in industries with known fluoride exposures, urinary analyses should prevent the occurrence of this crippling disorder. In the case of individuals drinking water containing excessive amounts of fluoride, analyses of the water supply and of the urine should make possible the control of this hazard.

Is There Danger of Chronic High-Grade Fluorosis? ---

The volume of 2 per cent sodium fluoride solution applied in a topical treatment as was stated, might be 2 cc. containing 20 mg. of fluorine. On the basis of the best available opinion, if this entire amount were swallowed and if the treatment were continued daily for ten to twenty years, crippling fluorosis might occur. Such a prospect is so fantastic that no further comment is needed.

The question might be raised as to the accumulation of fluoride. For example, if fruits and vegetables are sprayed with a fluoride insecticide and if they are cooked in a fluoride water (1 ppm.) in which the fluoride content is increased by evaporation of the water, and if the patient is drinking 1 ppm. fluoride water, and taking fluoride vitamin tablets containing 1 mg. of fluorine, and is using a fluoride dentifrice, would all of these sources of fluoride combine to exceed a limit of safety from crippling fluorosis? The answer, in our opinion, is negative. It is almost impossible to imagine any set of circumstances in which the fluoride intake might become sufficient to bring about chronic high-grade fluorosis, if the fluorine content of the water is of the order of 1 ppm.

Chronic Poisoning: Low-Grade

Since mottled enamel was first effectively described by Black and McKay in 1916, this disfiguring hypoplasia has been the object of continued and large-scale epidemiological study. The condition has been graded as to severity by Dean into six classes or, as distinct from "normal": (1) questionable -- a few white flecks in groups of about 25 children; (2) very mild -- small opaque paper white areas scattered irregularly, involving less than 25 per cent of the tooth surface; (3) mild--the areas involve at least half of the tooth surface and a few brown stains may occur; (4) moderate -- all of the tooth surface is involved with no change in tooth form, except minute pitting; brown stain is frequent; (5) moderately severe -- a greater depth of the enamel is involved; pitting is more frequent with brown stain, if present, generally deeper in hue. (6) severe -- hypoplasia so marked the form of the teeth is at times affected; pits are deeper and often confluent; stains are brown to chocolate or black.

The histogenesis of mottled enamel has been shown to involve more or less acutely hypoplastic and ultimately cuboidal ameloblasts. With the loss of form of the ameloblasts goes a loss of function so that, in advanced lesions, the ameloblast activity is almost entirely gone. The failure of the ameloblast produces the loss of tooth structure seen in severe mottling. At present, the origin of the stain is not understood. The interrod cement substance may be influenced as well as the formation of the rods themselves. The changes responsible for the opalescence and for the tiny white spots in the mild grades of mottling are likewise not understood. Since mottled enamel arises from interference with ameloblastic activity, it is obvious that the condition can be produced only during the first eight years of life when teeth are calcifying.

DeEds found in vitro depression of bone phosphatase activity by sodium fluoride in "one two-hundreth molar" concentration. This is of the order of 100 ppm. fluorine.

Daily Fluoride Intake Associated with Mottled Enamel---
H. V. Smith - - concluded from observations in Arizona:

The evidence indicates strongly that any water with a fluorine content of 0.9 ppm. (when analyzed by the Foster, Willard, or Sanchis methods)

or over is dangerous from the standpoint of probable damage to the teeth.

Badger has also reported cases of mottled enamel in children drinking from a community water supply in New Mexico containing 0.9 ppm. fluorine. But Dean, Jay, Arnold, McClure and Elvove reported only 47 per cent of the children of Galesburg, Illinois, "showed some form of mottled enamel generally of a very mild type. The remainder, 129, were classified as normal or questionable." The fluorine concentration of Galesburg water was twice that considered dangerous by Smith and Badger. The probable explanation of these differences lies in the hot, dry climate of Arizona and New Mexico compared to the relatively humid, cooler environment of Galesburg, Illinois. It is therefore, advisable to consider that in the fluoridization of water supplies, in the summer mottled enamel can be caused by fluorine at 1 ppm. whereas in the winter months a higher level may be tolerated.

The conclusions of Smith apparently early dominated the control of fluorides in water supplies as the drinking water standards for the United States were set tentatively at 1.0 ppm. fluorine as a maximum. An editorial referred to 1.0 ppm. as the permissible maximum. The limit for fluorine in water supplies were set at 1.5 ppm. in 1946. Enforcement of this arbitrary limit would call for modification or rejection of the water supply of Galesburg, Illinois.

The relationship between severity of mottling and the fluoride content of communal water supplies has been clearly established by the often quoted investigations of Dean and colleagues. Hodge has found a simple, linear relationship between the logarithm of the fluorine content of a community water supply and (a) the index of mottled enamel and (b) the reduction of dental caries. He has suggested that the point of intersection of the lines "might be called the 'point of minimum' caries with minimum mottled enamel' or the 'point of maximum usefulness of fluorides with minimum harm'."

The treatment of mottled enamel as an endemic disease obviously is a problem of prevention. Many cities carried out expensive procedures to lower the fluoride content in the drinking water to nonmottling levels following the demonstration in 1931 by Smith, Lantz and Smith, and independently by Churchill, that fluoride was responsible for this dystrophy. Where fluorine is present in waters at levels to cause mottled enamel two procedures are available: seek other sources of water or remove the fluorides. In either case the level of fluorides should not be reduced below 1 ppm. and it may be found advisable in many localities to leave the amount of fluorine at higher levels for most of winter, spring and fall. Therefore if the source of water is changed it may be advisable to blend the new water with the old to obtain the desired fluorine level.

Nichols has reviewed the methods of treatment of water to reduce the fluorine content. Two general procedures are available, namely, those based on reaction of the fluoride with hydroxyapatite, variously prepared, or with alumina. The latter reagent is of further importance since, if sodium aluminate treatment of water supplies is used, addition of sodium fluoride for caries prevention must be done after the lime flocculation. Otherwise an appreciable amount of the added fluoride will be lost.

To solve the esthetic problem for the victims of mottled enamel, local treatments are sometimes employed (Younger, reference 9, p. 50). However, porcelain facings, jacket crowns or even dentures may be required.

Is There a Danger of Mottled Enamel From Prophylactic Applications of Fluorine? --- When fluorides are added to public water supplies, the total fluoride content is usually set at 1 ppm. or slightly more. This concentration has been indicated as able to confer most of the reduction in dental caries attainable by the use of fluorides. From the charts shown by Hodge, it is clear that, on the average, the mottling in persons drinking such water will be less than the "very mild" category. It should be reiterated that in the community from which such an average figure is obtained, there will be a few persons who develop "very mild" or "mild" mottling. It is our opinion that this mottling will never be disfiguring.

What of the person drinking such water who receives fluoride in a topical application? The extra amount of fluorine ingested on the day of treatment may well be several milligrams but should not exceed 20 mg. Studies of the rate of excretion of fluorides indicate that a single dose of fluorides is rapidly excreted, so that the effects would not be produced after a day or two. Consequently, even a program of three or four applications at weekly intervals once or twice a year would not add enough fluoride to have any recognizable action. On the other hand, it is possible that persons drinking water containing 1 ppm. who also ingest fluoride tablets daily during the first eight years of life, might be able to increase the total fluoride absorbed by the body to the extent of producing disfiguring mottling. The amounts of fluoride that may be absorbed from the use of fluoride-containing dentifrices, mouth washes or chewing gum is not known at present so that these sources cannot be evaluated.

A possible future danger of mottled enamel lies in over-enthusiasm to provide fluorides for the prevention of dental caries. Proposals have been made for the use of bone meal because of its fluorine content, which may range up to 1,000 ppm. Fluoride-containing tablets are being sold. "The food in the diet will contribute on the average of 0.20-0.30 mg. of fluorine daily" but there are foods which have high fluorine content such as canned salmon, including bones, containing up to 6 ppm. and fish pastes with up to 9 ppm. McClure has recently summarized the data of the fluorine content of foods.

Safety of Prophylactic Application of Fluorine ---Hodges, Fareed, Ruggy and Chadnoff examined 86 persons from age 7 1/2 to 71 years in towns with fluorine from 1.2 to 3.0 ppm. in the water. They found no evidence by roentgenography of sclerosis of the skeleton.

Bone Fracture; Growth. --- McClure studies the relation of fluoride from water supplies to the height, weight and bone-fracture experience of 1,458 high school boys and 2,529 young men taking physical examinations at United States armed forces induction centers. The bone fractures were classified as (a) arm, wrist or elbow (b) collar bone (c) leg, knee or ankle (d) nose and (e) other. He concluded;

There was no relation of fracture experience to fluoride exposure. The average height and body weight of all the boys compared favorably with other height-weight data and accepted standards. The height-weight data were not related to fluoride exposures

While these data on bone-fracture experience for both men and boys of these ages do not permit final conclusions, they do suggest strongly, that no serious impairment in skeletal performance, as might be manifest in number of broken bones, seems related to exposure to fluoride domestic waters of the concentrations studies in this survey.

Texas men exposed to highest water-fluorine concentrations and Oklahoma men averaged 69.6 and 69.4 inches in height (weight 149.0 and 142.4 pounds), respectively. Men from rural Indiana and Indianapolis averaged 68.1 and 68.3 inches in height, 146.8 and 146.2 pounds in weight respectively, Washington, D.C., men averaged 69.3 inches and weighed 151.2 pounds on the average. New Hampshire men were 67.3 inches tall and weighed 149.6 pounds on the average. These height weight figures showed no relation to fluoride exposure.

Thyroid Metabolism --- Evans and Phillips reviewed the evidence of fluorine as influencing the course of hyperthyroidism. They analyzed thyroids of forty thyroidectomy cases for fluorine and iodine and compared the findings with the basal metabolic rates. They concluded: "The data obtained gave no definite evidence that fluorine in any way played a part in human hyperthyroidism by its action on the thyroid gland."

Effects on Hearing --- There is some possibility that fluorine of water supplies may have beneficial effects on hearing. Lewy found hearing defects in 4.9 per cent of 109,869 children from low fluorine districts in Illinois, and 2.8 per cent in 20,488 from districts with fluorine not over 1.4 ppm.

Mottled Enamel: A Delicate Sign. --- The appearance of mottled enamel appears to be the most delicate sign of chronic fluorine toxicity. In Table 2, some of the effects of minimum dosages of fluorine have been listed.

From the evidence available at present, a sample of which has been presented in Table 2, it appears that mottled enamel is the most delicate known effect of fluorides. As far as is known, there is no other toxic effect from ingesting amounts of fluoride as small as those taken when the drinking water contains 1 ppm. fluorine.

Table 2 - - - Minimum dosage of fluorine to produce various effects in animals -

Effect	Dosage	Species
Growth retardation	20 mg. /kg. /day	Rat
Growth retardation	313 ppm.	Rat
Growth retardation	2-3 mg. /kg. /day	Cat
Reduction in birth weight	190 ppm.	Rat
Milk yield decrease	2-3 mg. /kg. /day	Cow
Survival to weaning	226 ppm.	Rat
Calcium retention decreased	623 ppm.	Rat
Calcium balance unchanged	CaF_2 4-6 mg. /kg. /day	Pig
Bleached incisors	14 ppm. (added)	Rat
Striations of incisors	4 ppm. in water	Rat
Mottled enamel	1 ppm. in water	Human

Local Actions

Fluorides applied locally in high concentrations may have deleterious effects of importance to dentistry.

Topical Applications of Fluorides --- Abelson reported a case of dermatitis affecting the first two fingers and thumb of a dentist who had been using sodium fluoride for topical applications for six months. The attacks had occurred at the start of the applications but an attack resulting in blisters had occurred about three weeks prior to Abelson's observation of the case. A patch test with sodium fluoride gave a "late but plus 4 positive reaction."

Considering the small amounts of sodium fluoride actually used in recommended topical application procedures --- about 1 cc. of 2 per cent solution or about 10 mg. of fluorine -- there is no danger of any toxic sequelae. Consequently no precautionary measures are indicated such as a follow-up with calcium chloride solution or other calcium salts as used by Brady.

Possible Pulp Injury in Desensitizing Dentin. --- Barker used Lukomsky's paste in cavities and found it resulted in a large pulp abscess, fibrosis of the pulp, destruction of odontoblasts and thickening of blood vessels. Hoyt and Bibby following Lukomsky, found that when a 33 per cent sodium fluoride paste was used in cavity preparation it caused intense pain on contact with freshly exposed dentin.

Lefkowitz and Bodecker showed that crystals of sodium fluoride placed in artificial cavities in human teeth caused pulp abscesses and hyperemia. They indicated more severe effects in human teeth.

Rovelstad included sodium fluoride in various ways in cavities prepared in children's teeth. These teeth were then extracted, for orthodontic reasons, (a) immediately, (b) 18 hours and (c) one week after application. "All of the teeth to which the drug was applied evidenced some pulpal reaction, with the exception of these removed immediately after the drug application."

Injections of Concentrated Solutions of Sodium Fluoride for Pyorrhea. --- The ease of removal of tightly adherent masses of tartar from extracted teeth by aqueous solutions of hydrofluoric acid led Head to apply a less injurious fluoride solution to the exposed portions of teeth in patients suffering from pyorrhea. He described the preparation of a 23 per cent solution of ammonium bifluoride in water and the beneficial effects when this solution was "injected once or twice a week in pockets around loose teeth." No systemic or local injury was noted although Head warned that "care must be taken not to inject into fresh cuts, as such procedure will cause great pain". No other reports of this use of fluoride solution appeared until Lukomsky recommended a similar use of sodium fluoride.

Summary

1. The possible hazards attendant on the use of fluorides in dentistry have been discussed. The most important applications of fluoride at present are (a) fluoridization of water, (b) topical use of concentrated solutions, and (c) fluoride paste used to desensitize dentin. Other uses of fluoride are cited that

are, at present, not therapeutically important.

2. Two per cent solutions of sodium fluoride as used for topical applications are perfectly safe when the application is made in the dental office. The two per cent solution is too toxic to be kept in homes and should never be prescribed.
3. Chronic, crippling fluorosis will never appear as a result of dental uses of fluorides.
4. Mottled enamel, the most delicate sign of fluoride toxicity, will be found when fluoridization is carried out at about 1 ppm. of fluoride only in a very few individuals in whom very mild mottling will occur. No unesthetic marring of the teeth should occur.
5. Persons drinking communal water supplies containing about 1 ppm. fluorine conceivably might increase the fluoride intake by daily accessory fluoride administration to a level sufficient to cause mottled enamel.
6. There is no other known toxic effect of drinking water containing 1 ppm. fluorine than the "very mild" mottling of the teeth.
7. Repeated local applications of fluorides on soft tissues, for example, the skin of the fingers, has produced dermatitis in a single recorded case.
8. Concentrated preparations of sodium fluoride have been shown to produce pulpal reactions when applied to freshly cut dentin for desensitization.

TOXICOLOGICAL EVIDENCE FOR THE SAFETY OF THE FLUORIDATION OF PUBLIC WATER SUPPLIES*

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The extravagance of the variously motivated statements frequently heard in opposition to fluoridation wherever it is under consideration may lead officials who must explain this prophylactic measure to the public to discount the fact that many citizens still remain unconvinced of the safety of this procedure, despite the assurances of medical, dental, and public health authorities. Many are aware that a few scientists, physicians, and dentists, some of whom have contributed to our knowledge of the physiological effects of fluorides, have testified before a Congressional committee that, while not condemning fluoridation, they nevertheless hesitate to recommend its adoption at present. Unless public health authorities inform the public of the evidence upon which they base their belief in its safety, many persons will accept statements that little is known of the toxicity of fluorides and that the epidemiological evidence relied upon by the advocates of fluoridation fails to reveal adequately any adverse effects that may be associated with individual variations in susceptibility. For those who must present the subject a discussion of the present status of our knowledge of the toxicology of the fluoride ion may be helpful.

ACUTE TOXICITY

It is well known that inorganic fluorides are highly toxic, and that their use in the household as roach poisons has led to the poisoning of numbers of people into whose food they have been introduced accidentally. The study of acute poisoning has pertinence only in so far as it may reveal which organs are most vulnerable to the action of fluorides. The pathologic picture is one of hemorrhagic gastroenteritis and acute toxic nephritis, accompanied by more or less damage to the liver and other organs. Some of the signs and symptoms have been ascribed to a lowering of the blood calcium, but others result from the inhibitory action of the fluoride ion upon the activity of one or more enzymes that function in the sequence of reactions by which the energy of carbohydrates is made available for the metabolic activity of the tissues. The dose that is lethal when ingested by rabbits has been variously reported as ranging from 50 to 200 mg. of fluoride ion per kilogram of body weight. In human self-experimentation, as much as 250 mg. of sodium fluoride has been taken at one time without harm. It is evident that there need be no fear of the occurrence of acute poisoning as a result of the accidental or deliberate over-fluoridation of a water supply. Any toxic hazard that may be associated with fluoridation could be only that of the cumulative action of small amounts taken daily over a long period of time.

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CHRONIC TOXICITY

Chronic fluorosis was first described as occurring among animals. Darmor, an abnormality of the teeth and bones, occurs among sheep and cattle pastured in North Africa on land where the vegetation is contaminated by fluoride-bearing dusts derived from phosphate deposits. In Iceland, sheep grazing on pastures contaminated with fluoride-containing volcanic ash suffer from Gaddur, a condition in which the teeth are spotted, the bones are thickened, and the animals become lame and weak. Severe cases among sheep, goats, and cattle have occurred both in Europe and in the United States in the vicinity of factories that emit fluoride-containing compounds into the atmosphere. Such cattle have a stiff-legged gait, swollen hock-joints and palpable lumps on their bones as well as irregularly worn teeth.

Many experiments have been performed in the effort to reproduce the condition by incorporating fluorides in the food of rats, dogs, and other animals. Sheep, swine, and cattle, as well as chickens, have also been given fluoride-containing food in order to learn whether phosphate rock, which may contain from 3 to 4 per cent of fluoride, can be used safely as a mineral supplement in the feeding of livestock. Time is not available for a detailed discussion of these investigations, which have been reviewed by Roholm, McClure, Greenwood and DeEds. The continued daily ingestion by rats of diets containing from 7 to 12 ppm. induces signs of dental fluorosis, detectable only by means of a lens. When the diet contains somewhat greater amounts, the incisors become chalky, pitted, and corroded, and changes in the osseous system may result. Dietary levels of from 100 to 230 ppm inhibit growth. Rats that consume diets with 900 or more ppm die after a few weeks. Roholm, who expressed the intake in relation to body weight, concluded that incipient dental fluorosis may be induced by a daily intake of 1 mg. per kg. Five times that intake gave rise to incipient changes in the bones and kidneys, and one of from 10 to 15 mg. per kg. brought about recognizable signs of ill-health. Severe degenerative changes in the organs appeared when the daily intake was from 20 to 25 mg. per kg., and death occurred within a few days or weeks when it was 50 to 100 mg. per kg.

In our laboratory, Largent gave 65 mg. of fluorine daily to each of two 11-months-old littermate dogs, the third littermate serving only as control. It was given to one as sodium fluoride and to the other as cryolite, sodium aluminum fluoride. During the second month the dog given sodium fluoride lost appetite and vomited occasionally, but this did not persist. The administration of fluorides was continued for five years and five months, when it was stopped upon the death of the dog that had been given none. During life, no osseous changes could be detected roentgenographically. The ash of the bones of the dog given sodium fluoride contained 10 times the amount of fluoride found in the case of the dog used as control. Among the soft tissues, increased amounts were found only in the lungs and kidneys, which had 1.77 and 3.01 mg. per kg., respectively. No noteworthy histopathologic changes were found in the organs, and the bones, although chalky in appearance, exhibited no very striking abnormalities. The daily fluoride intake of these two dogs was of the order of 3 to 5 mg. per kg. In an experiment performed over 60 years ago, Brandl and Tappeiner gave as much as 10 mg. per kg. per day to a dog over the period of many months. Of the total of 402.9 grams of sodium fluoride given their dog, 330.5 gm. were recovered from the urine, and 64.6 gm. were found in the tissues, most of it in the bones.

Histological changes have occurred in the tissues of animals of several species following a daily intake great enough to retard growth. In Röhölm's experiments, the daily ingestion of 5 to 8 mg. per kg., by dogs have given rise to hematuria and albuminuria, with a histologic picture of degeneration of the epithelium of the kidney tubules, associated with interstitial contracting nephritis. Damage to the liver has been observed in some experiments, although less frequently. An intake of the order of 70 mg. per kg. is required in order to damage the gastric and duodenal mucosa.

Although diminished fertility has been reported in several experiments in which fluorides were fed to rats at a high dietary level, its occurrence may be regarded as secondary to the resulting poor growth or inanition, since rats behaved similarly, when limited to the amounts of a normal diet consumed voluntarily by those fed on fluoride-containing diets. Dietary levels near the threshold for the inhibition of growth did not affect the estrus cycle, although this ceased almost completely when the daily intake of fluoride was 25 mg. per kg.

Anemia has developed in severely poisoned dogs and a gel-like atrophy of the bone marrow has been induced in guinea pigs.

Although, in acute poisoning, the blood calcium may be lowered by about 50 per cent, it is decreased but slightly, if at all, in chronic poisoning. Retention by the bones of growing rats occurs normally unless the dietary content of fluoride is more than three or four hundred parts per million.

It may be concluded from the results of animal experimentation that interference with growth cannot be induced by a daily intake too small to give rise to dental abnormalities and that only after the bones have stored considerable quantities of fluoride does any impairment of skeletal function occur. Estimates by various investigators of the maximum daily intake in milligrams per kilogram of body weight that may be tolerated by animals of various species fall within the following ranges: dairy cattle, 1 to 3; swine, 5 to 12; rats, 10 to 20; guinea pigs, 12 to 20; chickens, 35 to 70. Such variations in susceptibility between species would make hazardous any attempt to predict the maximum safe human intake were there no observations upon the conditions as it occurs in man.

HUMAN FLUOROSIS FROM INDUSTRIAL EXPOSURE

Fluorosis is known to occur among workmen who inhale excessive amount of fluorides as dusts or vapors. In the course of the radiographic chest examinations of 78 Danish miners of cryolite, Møller and Gudjonsson found that 30 exhibited an abnormally increased density of the shadows of the spinal column, pelvis, and ribs. Some men complained of stiffness and pain in their joints, and in some cases the motility of the spine and thorax was reduced. In one man, ankylotic changes had occurred to a degree that caused severe functional impairment. Post-mortem examinations of two who died of inter-current disease revealed bones that were abnormally heavy and dense, chalky-white and marred by extensive periosteal deposits. The bones of these two persons contained many times the amounts of fluoride, 1 to 6 gm., normally present in human skeletons. The bones of one of them yielded 50 and those of the other 90 gm. of fluoride. The latter quantity had been deposited over a total of 7,500 working days, or an average rate of about 12 mg. per day. It was estimated that the amounts inhaled daily by these two men may have been of the order of 0.2 to 0.35 mg. per kg. of body weight. In neither case did the

organs show any histopathologic changes attributable to fluorides. There were, however, among the group as a whole many complaints of digestive disturbances and many of the workers were underweight and anemic.

Industrial fluorosis has occurred also in Germany and England, but only a very few cases have been reported in the United States. One was a 58-year old man who had long handled sodium fluoride and whose only complaints were of headache and fatigue. Another was discovered in a man with luetic aortitis who for 18 years had been exposed in a fertilizer factory to rock phosphate. On careful examination, a slight limitation of the motion of his lower spine could be detected, but he had no arthritic pains and no digestive disturbances. He was not anemic and his blood contained normal amounts of calcium and phosphorus.

HUMAN EXPERIMENTATION

In order to learn the rates at which storage in human bones occurs when known amount of fluorides are ingested daily, painstaking investigations in which six persons served as experimental subjects have been in progress for 12 years in our laboratory. By analyzing duplicate amounts of all the food and liquids ingested daily by them over prolonged periods, the average daily intake of fluoride of each subject has been measured. Two of these subjects were found to have ingested 0.49 and 0.72 mg. of fluorine per day, respectively. Within the limits of the accuracy of the sampling and the analyses of food materials and excreta, these persons appeared to be in metabolic balance with respect to fluoride. Subsequently, one of them ingested 6 mg. of extradietary fluoride (sodium salt) per day over a period, this amount being equivalent to 0.095 mg. per kg. of body weight. The amount absorbed into his tissues was determined by deducting from the measured intake the amount eliminated in his feces. An estimate of the amount retained in his body was obtained by deducting the amount excreted in the urine from the amount absorbed. This estimate was in error to the extent that fluoride may have been eliminated through the skin, which could not be measured in an experiment of long duration. When extradietary fluoride was taken as the soluble sodium salt, or when the less soluble calcium salt, was given in solution, 95 per cent of it was absorbed, but when it was given as a poorly soluble solid it was much less readily available, only 77 per cent of that given as cryolite or 37 per cent of that given as bone meal being absorbed. From brief balance experiments in which an attempt was made to measure the elimination through the skin, McClure concluded that when the daily intake did not exceed 4 or 5 mg., the major portion was eliminated from the body. That significant storage must have occurred during a period of 183 days on each of which 6 mg. was taken, however, was shown by the fact that for 11 weeks after this person ceased to take any extradietary fluoride, he continued to excrete considerably greater amounts than he ingested in his diet.

More recently, two persons have taken daily over long periods doses of the sodium salt that provided 3 and 12 mg. of fluoride, respectively, equivalent to 0.05 and to 0.14 mg. per kg. These dosages are well below those that Roholm believed capable of causing skeletal fluorosis. In neither of these persons have radiographic changes occurred in the density of the bones, although one of them took more than 20 gm. of sodium fluoride over a period of 120 weeks. Shortly after they began to take these amounts their urinary fluoride concentrations were 2 and 7 mg. per liter, respectively, but these tended to increase as the experiment progressed. At the start, the retention by the subject who took the lower dosage was 33.7 per cent, but between the 36th and 43rd weeks, it had decreased to 13.9 per cent. A similar trend toward decreasing rates of storage has been observed by others in the case of rats fed diets with either 4 or 12.5 ppm over 225 days.

HUMAN FLUOROSIS FROM WATER-BORNE FLUORIDES

From analyses of the water supplies of many communities in the United States, it has been estimated that over two million people use water with from 0.9 to 2.0 ppm and that three million use water with from 0.9 to 5.1 ppm. In a few areas even greater amounts are present. The chemical source of this naturally occurring fluoride is not known, but it is commonly assumed to be calcium fluoride. Our metabolic data have shown that when calcium fluoride is taken in solution the fluoride ion derived from it behaves as does that from sodium fluoride.

The daily intake of water varies widely with climatic conditions and with the individual, his age and activity. Normally active adults in temperate climate may drink from 1 to 3 liters, but those engaged in labor under desert conditions may require so much as 9 to 10 liters or even more. From many analyses of duplicates of the food and fluids consumed by a 63-year old man and his 57-year old wife, long-time residents of Bartlett, Tex., where the water contained 8 ppm, their average daily intake of fluoride was found to be 15.3 mg., only about 15 per cent of which appeared to be stored. Neither exhibited osseous changes. Their average urinary concentrations were 9.8 and 7.7 mg. per liter, respectively, values very closely approximating the concentration in the drinking water. These observations extend to higher concentrations and to greater ages, the earlier finding of McClure that the average urinary concentrations of groups of young men approximate closely those in the water they drank over the range of 0.2 to 4.7 ppm.

Chronic dental fluorosis occurs almost universally where the water contains 4 or more ppm, and very mild, difficultly detectable alterations in the enamel may be found in about 10 per cent of the children using water with 1 ppm. Belief in the inability of water having the latter concentration to induce the extra dental manifestations of fluorosis depends in part upon the extent to which these may be found when sought for among people using water containing greater amounts. Hodges found no evidence of skeletal fluorosis in x-rays of 31 persons who had lived for 18 to 68 years at Bureau, Ill., where the water has 2.5 ppm., or in those of 86 persons at Kempton, Ill., where the content has varied between 1.3 and 3 ppm. A radiologic survey of 114 persons who had lived for at least 15 years at Bartlett, Tex., where 8 ppm were present, revealed minimal evidence of an increase in the density of the bones of 12 per cent of those examined, but in no case was there any deformity or interference with function. Medical examinations, which included urinalyses and blood counts, revealed no evidence that the residents of Bartlett were less healthy than were those of nearby Cameron where the water contained only 0.3 ppm. Examination of 1,400 high school boys and 1,700 draftees, grouped in accordance with their residence in areas where the water contained 0.1, 0.5, 1.2 or 1.8 ppm, revealed no statistically significant differences in their heights and weights or in the numbers of fractures of bones suffered by them. In the Newburgh experiment on fluoridation as a preventive of dental caries, careful pediatric examinations have revealed no skeletal or other calcium and phosphorus metabolism of two girls with mottled enamel was found normal in balance experiments.

Reports of the endemic occurrence of skeletal fluorosis have, however, come from regions in other parts of the world where the water contains excessive amounts of fluoride, and where, as in India and China, malnutrition is prevalent. Only a few of these are complete enough to be of use in establishing the threshold concentration at which harm may occur. Six natives of South

Africa, who for 19 years had used water containing 11.8 ppm, exhibited characteristic radiographic changes and stiffness of the spine. In China, a few cases have occurred in persons who had used water containing 5.9, 6.3 or 13.1 ppm. No cases are known in which skeletal changes have occurred in regions where there is no mottling of the teeth.

More reliable quantitative information may be obtained by studying the condition as it arises from industrial exposure. Industrial hygienists determine the mean values and the ranges of the concentrations in which a noxious agent may appear in the urine among groups of workers exposed to various degrees of atmospheric concentration, and, by correlating the data with the presence or absence of illness among the various groups, learn which degrees of exposure are harmful and which are safe. The previously mentioned correspondence between the concentrations of fluorides in the urine and drinking water found among residents of various communities makes it possible to apply this method to data from industrial workers in an appraisal of the safety of fluoridation.

Healthy Danish workmen have urinary fluoride concentrations ranging from 0.3 to 1.6 mg. per liter, with a mean of 0.92 mg. per liter. In the group of cryolite workers which included many with skeletal fluorosis, the mean was 16 and the range 2.4 to 43.4 mg. per liter. In two factories in the United States, increases in the radiographic density of the bones have appeared in men, whose urine was known to have contained 10 or more mg. per liter. More recent data offer some indications that such changes may occur to a slight degree in a few men with urinary concentrations of but 6 mg. per liter.

Like other biological functions, the ability to excrete or to store fluorides may be expected to vary from individual to individual. The instances of early fluorosis of the bones seen among these workers and among a small proportion of the population of Bartlett suggest the threshold concentrations which may affect those persons who may be most prone to store fluoride.

It has been found that the ability of rabbits to excrete administered fluoride is diminished temporarily during the acute state of nephritis induced by giving nephrotoxic agent such as uranium.

The only case in which skeletal fluorosis in the United States has been attributed to water-bone fluoride was discovered incidentally during the illness of a 22-year old man who died of uremia seven years after he had suffered an accidental kidney injury. At necropsy, his right kidney was found to be but a thin-walled, cystic, fluid-filled mass, while the left was small and contracted. During the first seven years of his life he had used water containing 12 ppm. Later, he moved about living, with the exception of two years, in areas where the water contained 4.4 or 5.7 ppm. A somewhat similar case has been reported from South America.

In order to learn something of the rates at which fluoride may be stored by persons with kidney disease, it is suggested that a search be made for evidence of skeletal fluorosis in such x-rays as may be found in the case records of patients with chronic nephritis in hospitals in communities where the water contains known amounts of fluorides. In the unlikely event that evidence of the occurrence of fluorosis should be found in patients with chronic nephritis who have used water with no more than 1 ppm, it should be possible for physicians who discover such disease to advise their patients to use nonfluoridated water, which could readily be made available for their use. No evidence exists that water-borne fluoride has been a cause of nephritis. In examinations of many

specimens of the urine of young men who used water with from 2.0 to 5.0 ppm McClure found no more instances of the presence of blood or of albumin than were encountered among those using water with no more than 0.3 ppm. Examination of the mortality rates from nephritis, or other diseases, including cancer, recorded in various communities has revealed no association with the fluoride content of their water supplies.

CONCLUSIONS

The results of animal experimentation show that the prolonged intake of quantities of fluoride too small to induce dental fluorosis does not give rise to any of the nondental manifestations of chronic intoxication by fluorides. Epidemiologic data and clinical and radiographic examination of exposed industrial workers indicate that only when the fluoride content of a water supply exceeds 5 or 6 ppm will its prolonged usage give rise to detectable osseous changes and then only in the most susceptible persons. The evidence as a whole is consistent in offering assurance that bringing the fluoride concentration in communal water supplies to that known to be optimal for dental health is a prophylactic public health procedure which has an ample margin of safety.

